

AMENDMENTS

Please amend the claims as follows.

Please cancel claims 7 and 71.

1. (Currently amended) A method of determining a comparative expression profile in an individual, comprising:

- (a) creating a multidimensional space of n dimensions, wherein n represents the number of molecules being analyzed in a specimen from each individual in a population of reference individuals and wherein said multidimensional space contains n axes, each of said axes relating to the expression level of a molecule of said n molecules;
- (b) determining a multidimensional coordinate point for each individual in said population of reference individuals, wherein said multidimensional coordinate point is representative of the expression levels of said n molecules in the individual;
- (c) determining in said multidimensional space a health-associated reference expression region for said multidimensional coordinate points determined for said population of reference individuals;
- (d) contacting a specimen from an individual with a target;
- (e) determining the expression levels of a sample of n molecules in a population of molecules in said specimen from said individual;
- (f) determining a multidimensional coordinate point representative of the expression levels of said sample of n molecules in said specimen from said individual determined in step (e);
- (g) comparing said multidimensional coordinate point determined in step (f) to said health-associated reference expression region determined in step (c);
- (h) determining if said multidimensional coordinate point is within or outside said health-associated reference expression region, wherein said multidimensional coordinate point

within said health-associated reference expression region indicates a reference expression profile and wherein said multidimensional coordinate point outside said health-associated reference expression region indicates a perturbed expression profile, wherein said perturbed expression profile indicates a disease state in said individual; and

- (i) providing an output of said expression profile determined in step (h) to a user.

Claims 2-5 (Canceled).

6. (Original) The method of claim 1, wherein said reference expression profile indicates a reference health state in said individual.

Claim 7 (Canceled).

8. (Original) The method of claim 1, wherein said perturbed expression profile indicates the course of a disease.

9. (Original) The method of claim 1, wherein said specimen is selected from the group consisting of leukocytes, blood, and serum.

Claim 10 (Canceled).

11. (Original) The method of claim 1, wherein said molecules in said specimen comprise nucleic acids.

Claim 12 (Canceled).

13. (Original) The method of claim 1, wherein said molecules in said specimen comprise polypeptides.

Claim 14 (Canceled).

15. (Original) The method of claim 1, wherein said molecules in said specimen comprise small molecules.

16. (Original) The method of claim 1, further comprising the step of reporting whether a reference expression profile or a perturbed expression profile is indicated.

Claims 17-64 (Canceled).

65. (Currently amended) A method of diagnosing a health state, comprising:

- (a) creating a multidimensional space of n dimensions, wherein n represents the number of molecules being analyzed in a specimen from each individual in a population of reference individuals and wherein said multidimensional space contains n axes, each of said axes relating to the expression level of a molecule of said n molecules;
- (b) determining a multidimensional coordinate point for each individual in said population of reference individuals, wherein said multidimensional coordinate point is representative of the expression levels of said n molecules in the individual;
- (c) determining in said multidimensional space a health-associated reference expression region for said multidimensional coordinate points determined for said population of reference individuals;
- (d) contacting a specimen from an individual with a target;
- (e) determining the expression levels of a sample of n molecules in a population of molecules in said specimen from said individual;
- (f) determining a multidimensional coordinate point representative of the expression levels of the n molecules determined in step (e);
- (g) comparing said multidimensional coordinate point determined in step (f) with said health-associated reference expression region determined in step (c);
- (h) determining if said multidimensional coordinate point is within or outside said health-associated reference expression region, wherein said multidimensional coordinate point within said health-associated reference expression region indicates a reference health state and wherein said multidimensional coordinate point outside said health-associated reference expression region indicates a disease state in said individual; and
- (i) providing an output of said health state determined in step (h) to a user.

Claims 66-69 (Canceled).

70. (Original) The method of claim 65, wherein said reference expression profile indicates a reference health state in said individual.

Claim 71 (Canceled).

72. (Currently amended) The method of claim 65, wherein said ~~perturbed expression profile multidimensional coordinate point outside said health-associated reference expression region~~ indicates the course of a disease.

73. (Original) The method of claim 65, wherein said specimen is selected from the group consisting of leukocytes, blood, and serum.

74. (Previously presented) The method of claim 65, wherein the expression levels of said n molecules are determined by contacting said specimen with an array and measuring the expression levels of said n molecules.

75. (Original) The method of claim 65, wherein said molecules in said specimen comprise nucleic acids.

76. (Previously Presented) The method of claim 74, wherein said array comprises nucleic acid ligands.

77. (Original) The method of claim 65, wherein said molecules in said specimen comprise polypeptides.

78. (Previously presented) The method of claim 77, wherein the expression levels of said n molecules are determined by contacting said specimen with ligands, wherein said ligands are antibodies, and measuring the expression levels of said n molecules.

79. (Original) The method of claim 65, wherein said molecules in said specimen comprise small molecules.

80. (Original) The method of claim 65, further comprising the step of reporting whether a reference expression profile or a perturbed expression profile is indicated.

Claims 81-89 (Canceled).

90. (Currently amended) A method of diagnosing a health state in an individual, comprising:

- (a) creating a multidimensional space of n dimensions, wherein n represents the number of molecules being analyzed in a specimen from each individual in a population of reference individuals and wherein said multidimensional space contains n axes, each of said axes relating to the expression level of a molecule of said n molecules;
- (b) determining a multidimensional coordinate point for each individual in said population of reference individuals, wherein said multidimensional coordinate point is representative of the expression levels of said n molecules in the individual;
- (c) determining in said multidimensional space a health-associated reference expression region for said multidimensional coordinate points determined for said population of reference individuals;
- (d) contacting a specimen from an individual with a target;
- (e) determining the expression levels of a sample of n molecules in a population of molecules in said specimen from said individual by measuring the expression level of said n molecules in said specimen;
- (f) determining a multidimensional coordinate point representative of the expression levels of the n molecules determined in step (e);
- (g) comparing said multidimensional coordinate point determined in step (f) with said health-associated reference expression region determined in step (c);
- (h) determining if said multidimensional coordinate point is within or outside said health-associated reference expression region, wherein said multidimensional coordinate point within said health-associated reference expression region indicates a reference health state and wherein said multidimensional coordinate point outside said health-associated reference

expression region indicates a perturbed health state, thereby diagnosing the health state of said individual; and

- (i) providing an output of said health state determined in step (h) to a user.

Claims 91-94 (Canceled).

95. (Original) The method of claim 90, wherein said perturbed health state indicates a disease state in said individual.

96. (Currently amended) The method of claim 90, wherein said perturbed expression profile health state indicates the course of a disease.

97. (Original) The method of claim 90, wherein said specimen is selected from the group consisting of leukocytes, blood, and serum.

98. (Previously presented) The method of claim 90, wherein the expression levels of said n molecules are determined by contacting said specimen with an array and measuring the expression levels of said n molecules.

99. (Original) The method of claim 90, wherein said molecules in said specimen comprise nucleic acids.

100. (Previously Presented) The method of claim 98, wherein said array comprises nucleic acid ligands.

101. (Original) The method of claim 90, wherein said molecules in said specimen comprise polypeptides.

102. (Previously presented) The method of claim 101, wherein the expression levels of said n molecules are determined by contacting said specimen with ligands, wherein said ligands are antibodies, and measuring the expression levels of said n molecules.

103. (Original) The method of claim 90, wherein said molecules in said specimen comprise small molecules.

104. (Original) The method of claim 90, further comprising the step of reporting whether a reference expression profile or a perturbed expression profile is indicated.

Claims 105-137 (Canceled).

138. (Currently amended) A computer apparatus, comprising:

a processor;

main memory in communication with said processor; and

a comparative expression profiler in communication with said main memory configured to carrying out the computer-executed steps of:

(a) creating a multidimensional space of n dimensions, wherein n represents the number of molecules being analyzed in a specimen from each individual in a population of reference individuals and wherein said multidimensional space contains n axes, each of said axes relating to the expression level of a molecule of said n molecules;

(b) determining a multidimensional coordinate point for each individual in said population of reference individuals, wherein said multidimensional coordinate point is representative of the expression levels of said n molecules in the individual;

(c) determining in said multidimensional space a health-associated reference expression region for said multidimensional coordinate points determined for said population of reference individuals;

(d) determining a multidimensional coordinate point representative of the expression levels of a sample of n molecules from an individual; and

(e) comparing said multidimensional coordinate point determined in step (d) with said health-associated reference expression region determined in step (c), wherein said multidimensional coordinate point within said health-associated reference expression region indicates a reference expression profile and wherein said multidimensional coordinate point

outside said health-associated reference expression region indicates a perturbed expression profile, wherein said perturbed expression profile indicates a disease state.

139. (Original) The computer apparatus of claim 138, wherein said comparative expression profiler further is configured to carry out the computer-executed step of determining said expression level of said molecule.

Claim 140 (Canceled).

141. (Currently amended) A computer-readable medium having stored thereon a plurality of sequences of instructions, said plurality of sequences of instructions including sequences of instructions which, when executed by a processor, cause said processor to perform the steps of:

- (a) creating a multidimensional space of n dimensions, wherein n represents the number of molecules being analyzed in a specimen from each individual in a population of reference individuals and wherein said multidimensional space contains n axes, each of said axes relating to the expression level of a molecule of said n molecules;
- (b) determining a multidimensional coordinate point for each individual in said population of reference individuals, wherein said multidimensional coordinate point is representative of the expression levels of said n molecules in the individual;
- (c) determining in said multidimensional space a health-associated reference expression region for said multidimensional coordinate points determined for said population of reference individuals;
- (d) determining a multidimensional coordinate point representative of the expression levels of a sample of n molecules from an individual; and
- (e) comparing said multidimensional coordinate point determined in step (d) with said health-associated reference expression region determined in step (c), wherein said multidimensional coordinate point within said health-associated reference expression region indicates a reference expression profile and wherein said multidimensional coordinate point

outside said health-associated reference expression region indicates a perturbed expression profile, wherein said perturbed expression profile indicates a disease state.

Claims 142-143 (Canceled).

144. (Currently amended) A method of diagnosing a health state in an individual, comprising:

- (a) creating a multidimensional space of n dimensions, wherein n represents the number of molecules being analyzed in a specimen from each individual in a population of reference individuals and wherein said multidimensional space contains n axes, each of said axes relating to the expression level of a molecule of said n molecules;
- (b) determining a multidimensional coordinate point for each individual in said population of reference individuals, wherein said multidimensional coordinate point is representative of the expression levels of said n molecules in the individual;
- (c) determining in said multidimensional space a health-associated reference expression region for said multidimensional coordinate points determined for said population of reference individuals;
- (d) contacting a leukocyte specimen from an individual with a target;
- (e) determining the expression levels of a sample of n molecules in a population of molecules in said leukocyte specimen by measuring the expression level of said n molecules in said specimen;
- (f) determining a multidimensional coordinate point representative of the expression levels of the n molecules determined in step (e);
- (g) comparing said multidimensional coordinate point determined in step (f) with said health-associated reference expression region determined in step (c);
- (h) determining if said multidimensional coordinate point is within or outside said health-associated reference expression region, wherein expression levels within said

health-associated reference expression region indicates a reference health state and wherein expression levels outside said health-associated reference expression region indicates a perturbed health state, thereby diagnosing the health state of said individual: and

(i) providing an output of said health state determined in step (h) to a user.

145. (Previously presented) The method of claim 144, wherein said perturbed health state indicates a disease state in said individual.

146. (Currently amended) The method of claim 144, wherein said perturbed expression profile health state indicates the course of a disease.

147. (Previously presented) The method of claim 144, wherein said target is an array.

148. (Previously presented) The method of claim 144, wherein said molecules in said specimen comprise nucleic acids.

149. (Previously presented) The method of claim 144, wherein said target comprises nucleic acid ligands.

150. (Previously presented) The method of claim 144, wherein said molecules in said specimen comprise polypeptides.

151. (Previously presented) The method of claim 144, wherein said target comprises ligands, wherein said ligands are antibodies.

152. (Previously presented) The method of claim 144, wherein said molecules in said specimen comprise small molecules.

153. (Previously presented) The method of claim 144, further comprising the step of reporting whether a reference expression profile or a perturbed expression profile is indicated.

154. (Previously presented) The method of claim 1, wherein n is 3 or more molecules.

155. (Previously presented) The method of claim 1, wherein n is 5 or more molecules.

156. (Previously presented) The method of claim 1, wherein n is 10 or more molecules.

157. (Previously presented) The method of claim 1, wherein n is 20 or more molecules.
158. (Previously presented) The method of claim 1, wherein n is 50 or more molecules.
159. (Previously presented) The method of claim 1, wherein n is 100 or more molecules.
160. (Previously presented) The method of claim 1, wherein n is 200 or more molecules.
161. (Previously presented) The method of claim 1, wherein n is 500 or more molecules.
162. (Previously presented) The method of claim 1, wherein n is 1000 or more molecules.
163. (Previously presented) The method of claim 65, wherein n is 3 or more molecules.
164. (Previously presented) The method of claim 65, wherein n is 5 or more molecules.
165. (Previously presented) The method of claim 65, wherein n is 10 or more molecules.
166. (Previously presented) The method of claim 65, wherein n is 20 or more molecules.
167. (Previously presented) The method of claim 65, wherein n is 50 or more molecules.
168. (Previously presented) The method of claim 65, wherein n is 100 or more molecules.
169. (Previously presented) The method of claim 65, wherein n is 200 or more molecules.
170. (Previously presented) The method of claim 65, wherein n is 500 or more molecules.
171. (Previously presented) The method of claim 65, wherein n is 1000 or more molecules.
172. (Previously presented) The method of claim 90, wherein n is 3 or more molecules.
173. (Previously presented) The method of claim 90, wherein n is 5 or more molecules.

174. (Previously presented) The method of claim 90, wherein n is 10 or more molecules.
175. (Previously presented) The method of claim 90, wherein n is 20 or more molecules.
176. (Previously presented) The method of claim 90, wherein n is 50 or more molecules.
177. (Previously presented) The method of claim 90, wherein n is 100 or more molecules.
178. (Previously presented) The method of claim 90, wherein n is 200 or more molecules.
179. (Previously presented) The method of claim 90, wherein n is 500 or more molecules.
180. (Previously presented) The method of claim 90, wherein n is 1000 or more molecules.
181. (Previously presented) The method of claim 144, wherein n is 3 or more molecules.
182. (Previously presented) The method of claim 144 , wherein n is 5 or more molecules.
183. (Previously presented) The method of claim 144 , wherein n is 10 or more molecules.
184. (Previously presented) The method of claim 144 , wherein n is 20 or more molecules.
185. (Previously presented) The method of claim 144 , wherein n is 50 or more molecules.
186. (Previously presented) The method of claim 144, wherein n is 100 or more molecules.
187. (Previously presented) The method of claim 144, wherein n is 200 or more molecules.

188. (Previously presented) The method of claim 144 , wherein n is 500 or more molecules.

189. (Previously presented) The method of claim 144 , wherein n is 1000 or more molecules.